



# Clinical Benefit of Evolocumab in Patients with a History of MI: An Analysis from FOURIER

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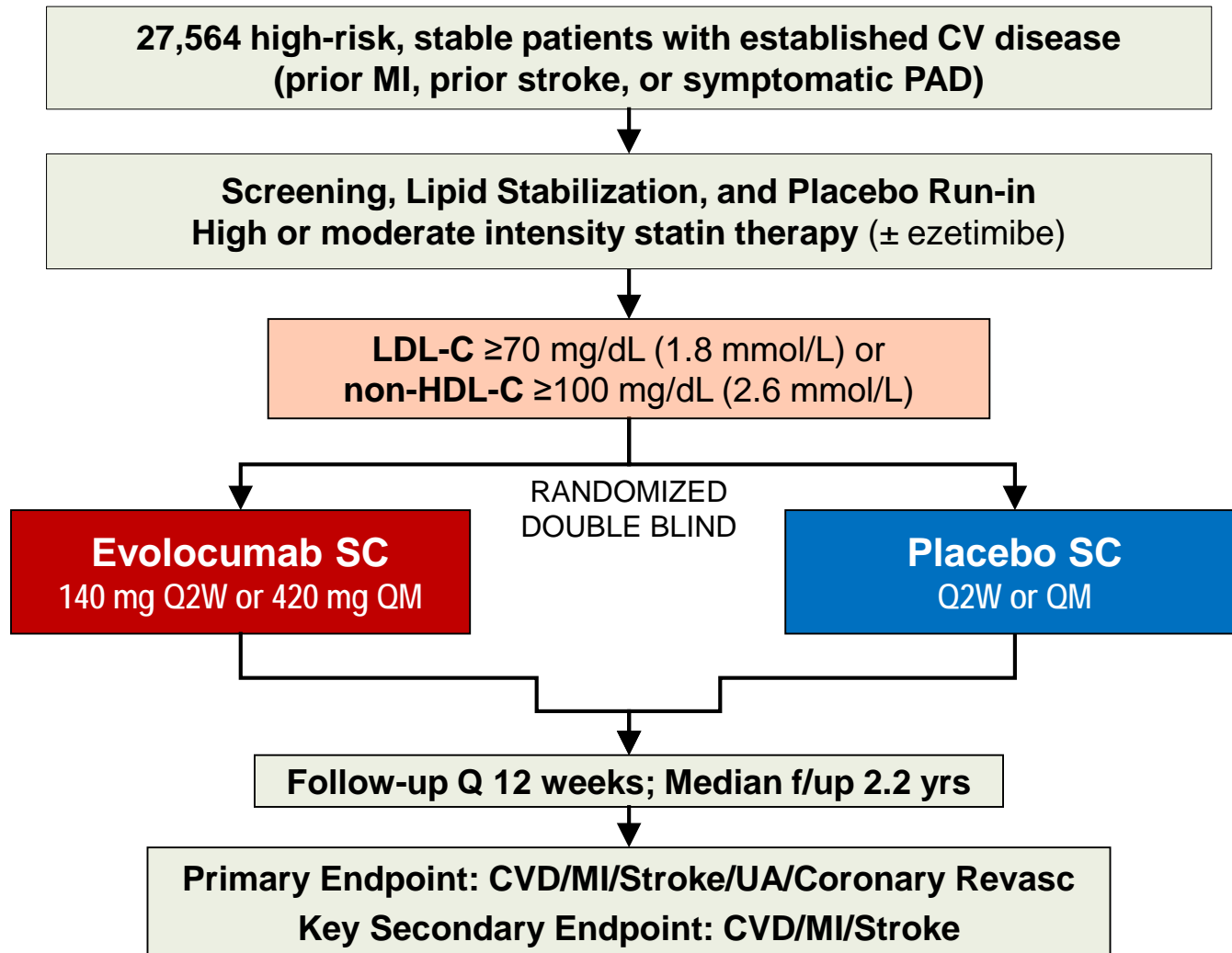
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An Academic Research Organization of  
Brigham and Women's Hospital and Harvard Medical School



# Trial Design

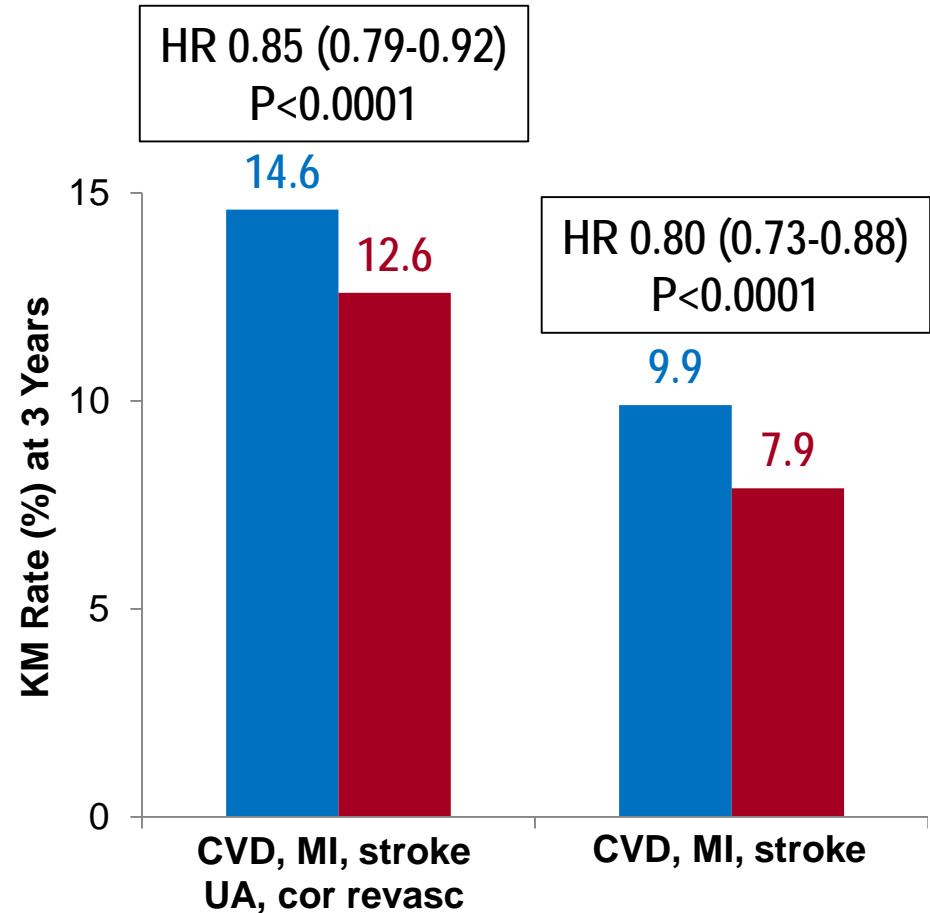
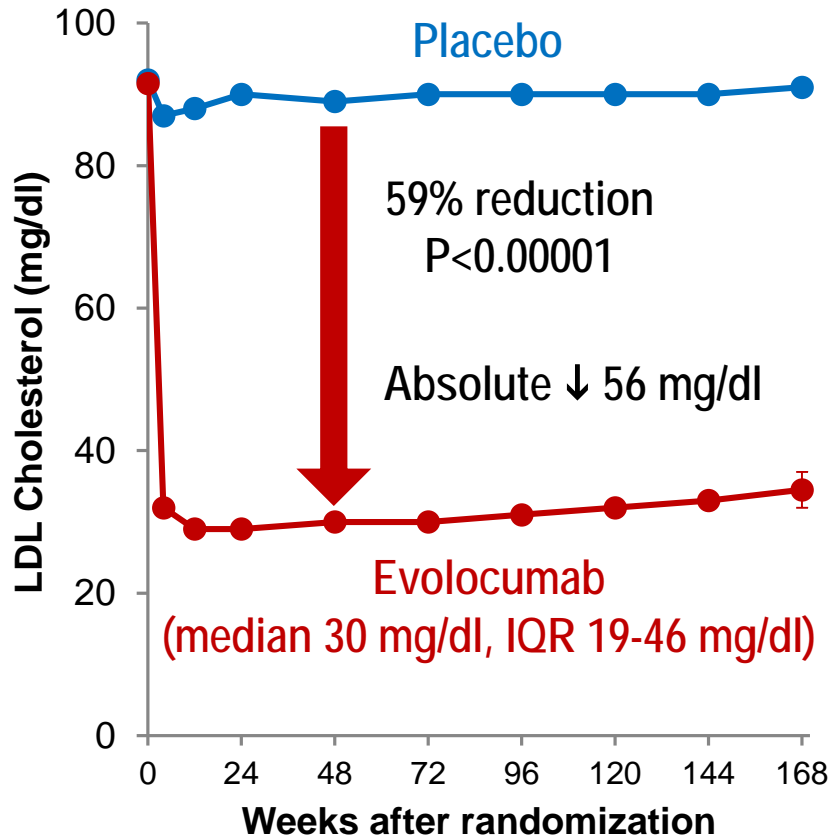




# Summary of Effects of PCSK9i Evolocumab



- ↓ LDL-C by 59% down to a median of 30 mg/dl
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated





# Background & Objective



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**Patients at higher CV risk may derive greater benefit from PCSK9 inhibition**

**Within the broad subgroup of patients w/ prior MI in FOURIER, we investigated if readily ascertainable clinical features of the CAD history identified patients:**

- 1) At higher CV risk**
- 2) Who derived greater benefit from PCSK9 inhibition**





# High-Risk Features in Patients with History of MI



21,162 patients with prior MI randomized to ticagrelor vs. placebo on a background of aspirin

	Subgroup	Placebo Arm 3-yr KM Rate of CVD/MI/Stroke	Relative Risk Reduction	Absolute Risk Reduction
	All patients	9.0%	16%	1.3%
Time from prior MI	<2 yrs	9.7%	23%	2.0%
	≥2 yrs	7.9%	4%	0.4%
# of prior MIs	≥2 MI's	15.2%	15%	1.6%
	1 MI	7.8%	17%	1.2%
Multivessel CAD	MVD	9.4%	19%	1.6%
	No MVD	8.6%	12%	0.9%

Bonaca MP et al. *NEJM* 2015;372:1791-1800

Dellborg M et al. *ESC* 2017

Bonaca MP et al. *JACC* 2017;70:1368-75

Bansilal S et al. *JACC* 2016;67(Suppl):2146





# Methods



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- **Analyses restricted to 22,351 Pts w/ prior MI**
  - **Divided into subgroups on basis of 3 factors** (all of which were prespecified enrichment risk factors):
    - Time from qualifying MI
    - # of prior MI's at baseline
    - Presence of residual multivessel disease at baseline
  - **Outcome of interest: CV death, MI, or stroke**
  - **Analyses**
    - Risk of CV events in placebo arm in patients w/ or w/o a specific high-risk feature
    - Efficacy of evolocumab vs. placebo within each subgroup



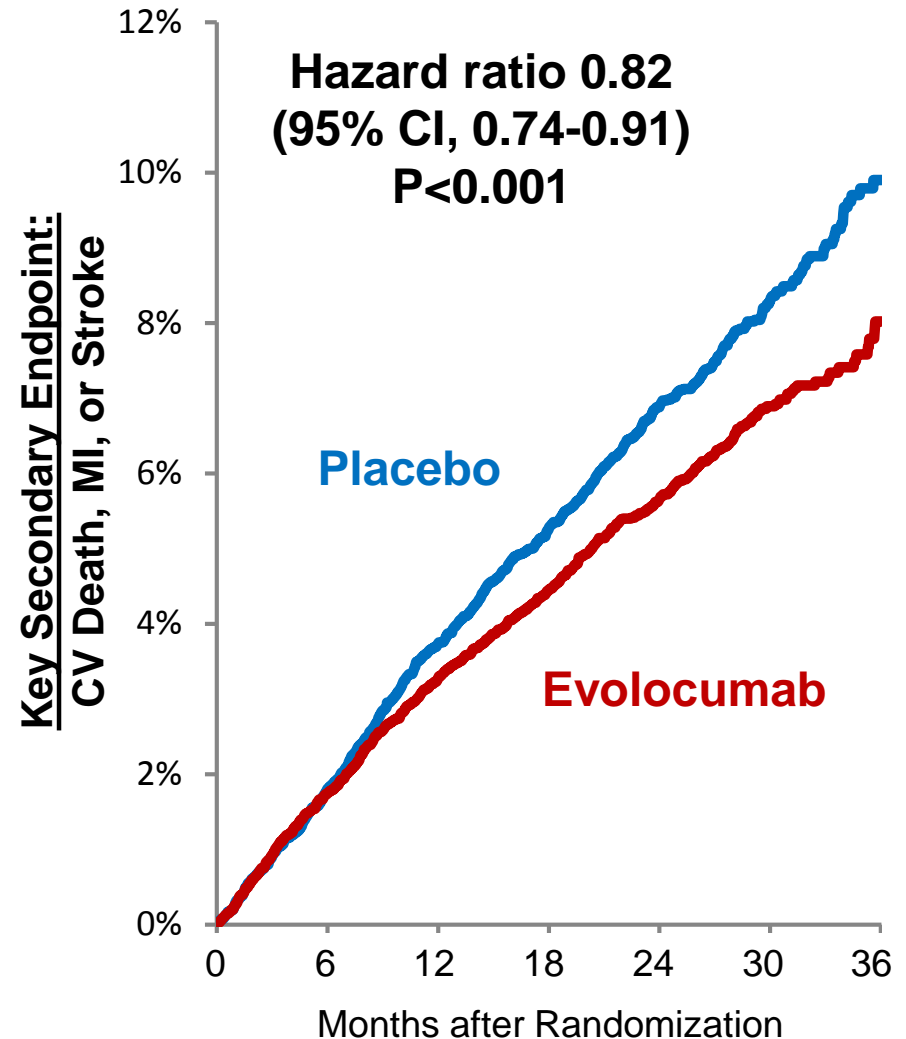


# Prior MI Overall



22,351 patients (81% of overall trial)

Characteristic	Value
Age, mean (SD)	62 (9)
Male sex (%)	78
Hypertension (%)	79
Diabetes mellitus (%)	35
Current smoker (%)	28
High-intensity statin (%)	71
LDL-C, mg/dL (IQR)	92 (80-109)
LDL-C w/ EvoMab at 48 wk, mg/dL (IQR)	30 (19-46)





# High-Risk Features and Other Baseline Characteristics



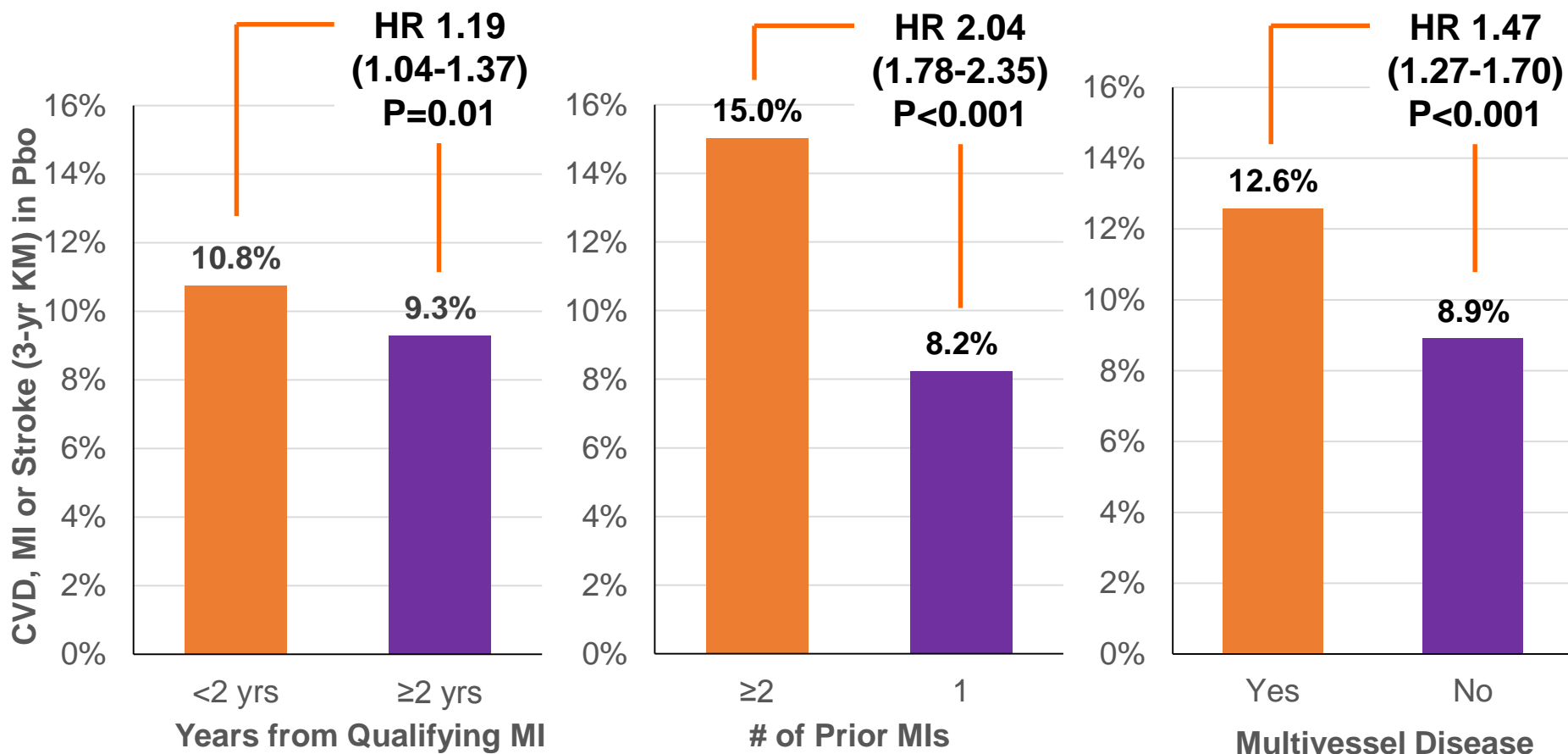
Characteristic	Time from Qualifying MI		# Prior MIs		Residual Multivessel CAD	
	<2 y ago N=8402 (38%)	≥2 y ago N=13,918 (62%)	≥2 N=5285 (24%)	1 N=17,047 (76%)	MVD N=5618 (25%)	No MVD N=16,715 (75%)
Age, mean (SD)	60 (9)	63 (9)	62 (9)	62 (9)	62 (9)	62 (9)
Male sex (%)	77	79	82	77	81	78
Hypertension (%)	75	81	81	78	82	78
Diabetes mellitus (%)	31	38	36	35	35	35
Current smoker (%)	28	28	26	28	26	28
High-intensity statin (%)	76	69	75	70	74	70
LDL-C, mg/dL (IQR)	90 (79-106)	93 (80-110)	92 (81-105)	92 (80-108)	93 (81-110)	92 (80-108)
LDL-C w/ EvoMab at 48 wk, mg/dL (IQR)	29 (19-45)	30 (18-46)	30 (19-46)	29 (19-46)	30 (19-46)	29 (18-46)







# Risk of CV Death, MI or Stroke with Each Risk Factor





# Multivariable Adjusted Analyses of All 3 Factors



Risk Factor	Adjusted HR (95% CI) for CV death, MI or stroke	P value
Qualifying MI <2 y ago	1.36 (1.18-1.57)	<0.001
≥2 Prior MIs	1.90 (1.65-2.19)	<0.001
Residual multivessel CAD	1.34 (1.16-1.55)	<0.001

Model in placebo arm of trial includes all 3 risk factors plus the following covariates: age, sex, weight, race, region, h/o stroke, h/o PAD, HTN, DM, current smoking, eGFR ≥60, high-intensity statin use, and LDL-C at baseline.

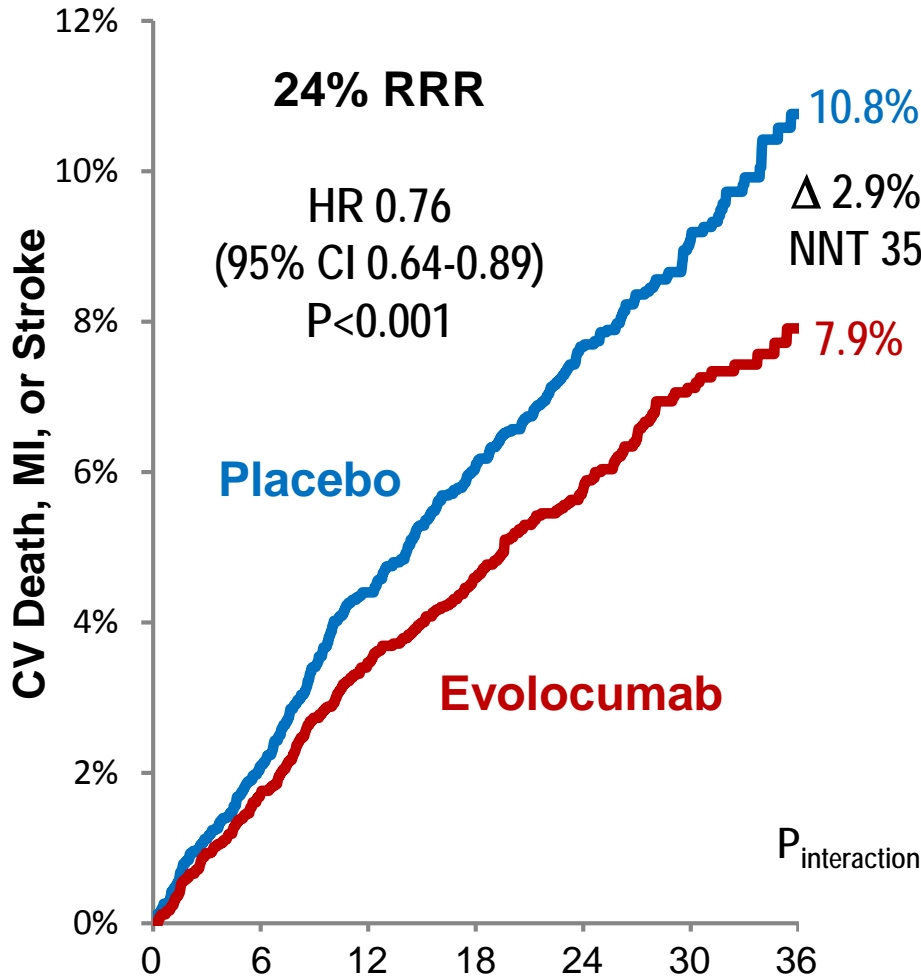




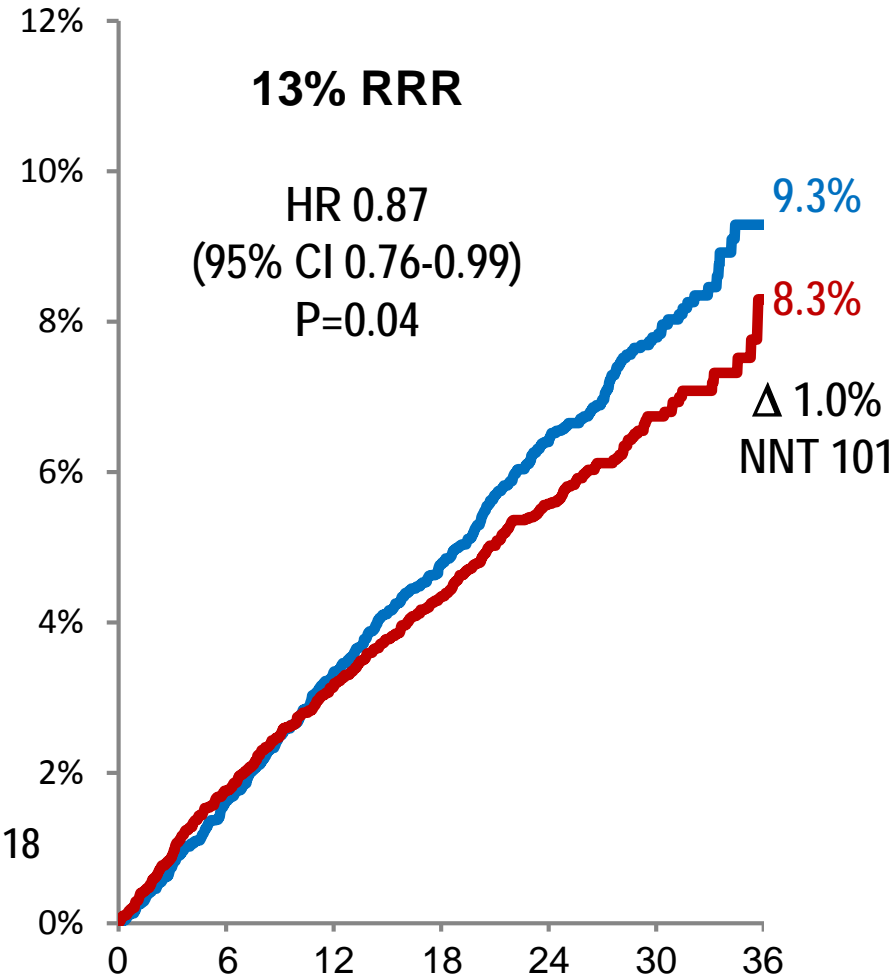
# Benefit of EvoMab Based on Time from Qualifying MI



## Qualifying MI <2 yrs ago



## Qualifying MI $\geq$ 2 yrs ago

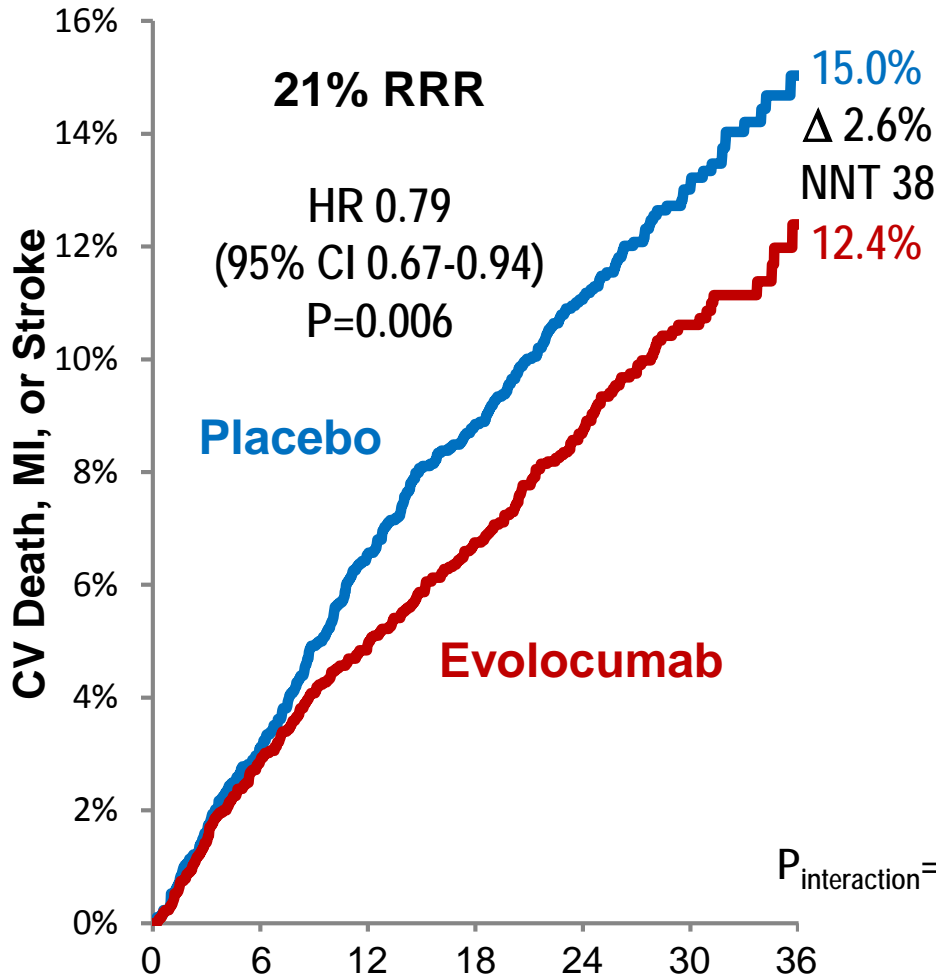




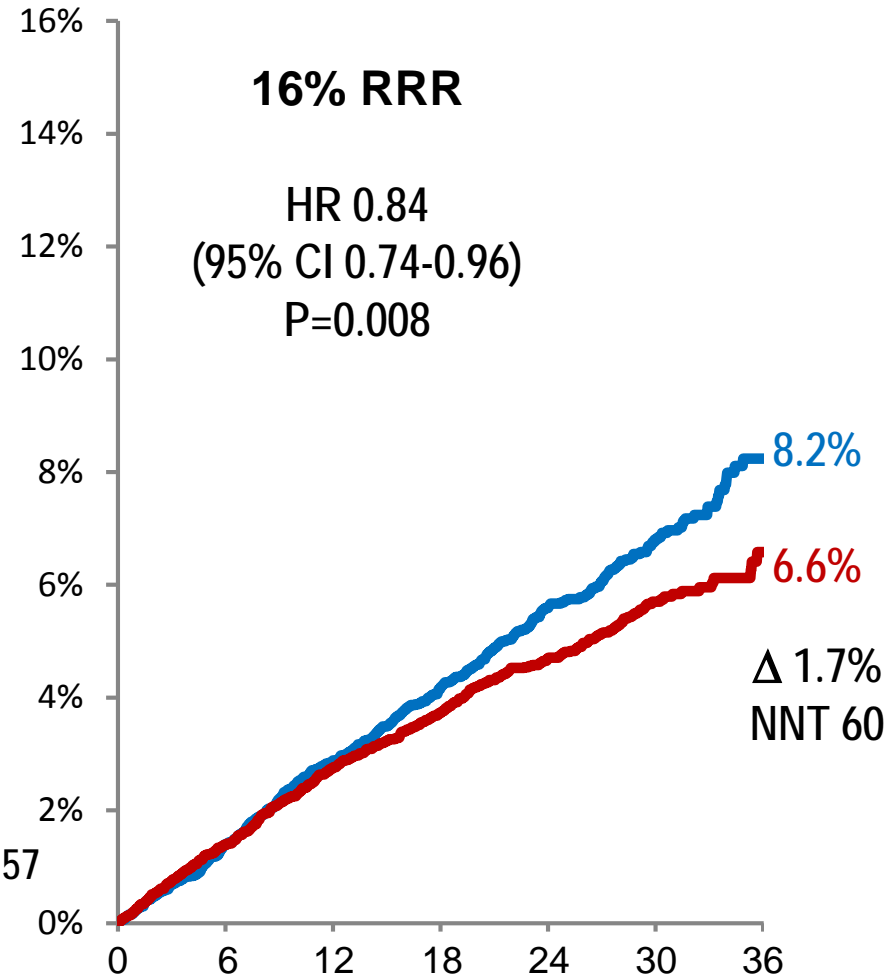
# Benefit of EvoMab Based on # of Prior MIs



## ≥2 Prior MIs



## 1 Prior MI

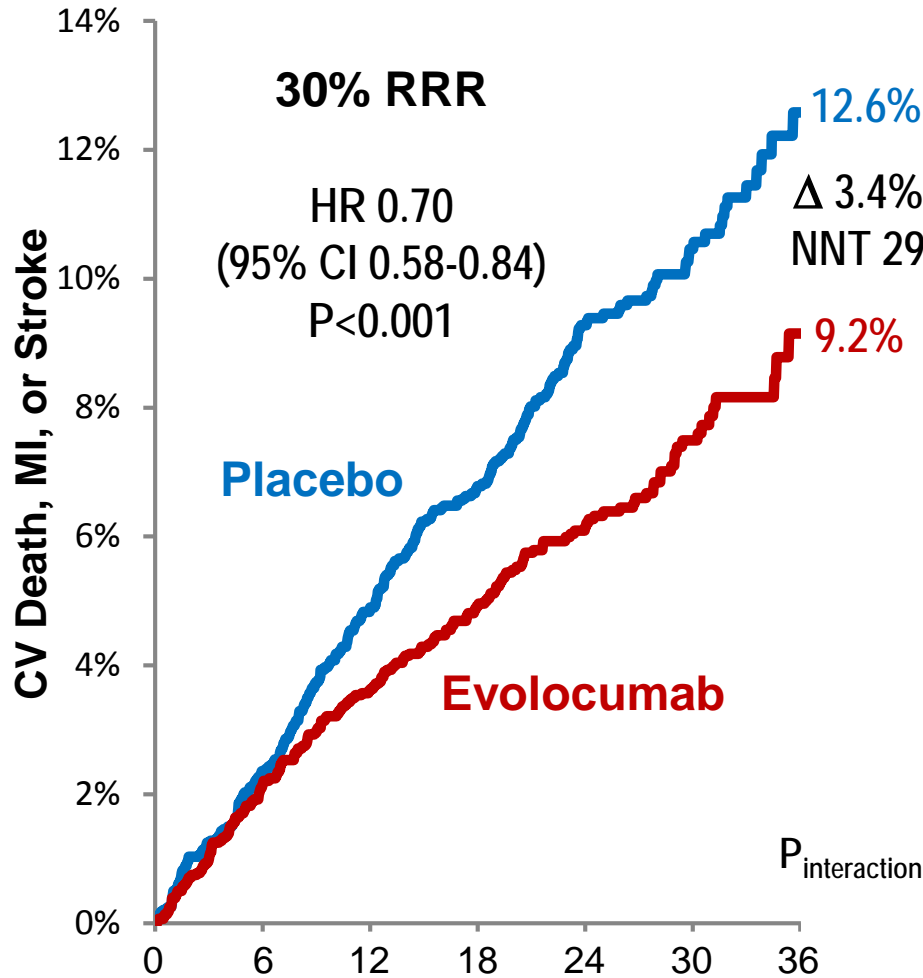




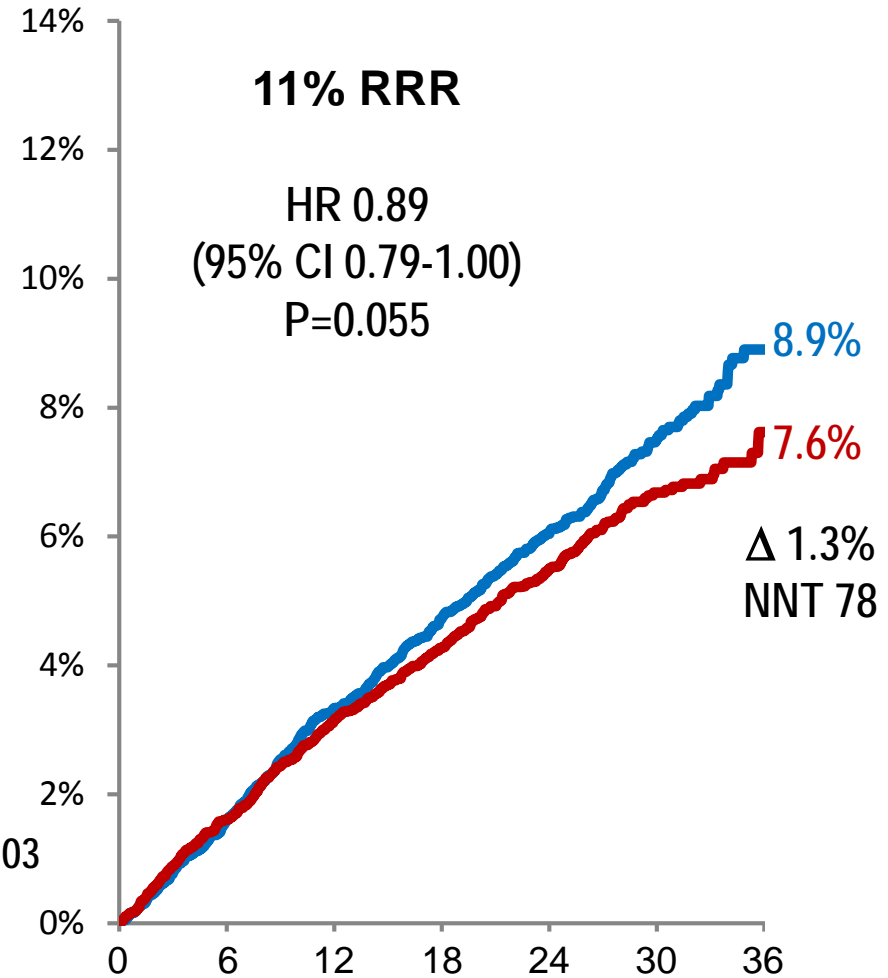
# Benefit of EvoMab Based on Multivessel Disease



## Multivessel Disease

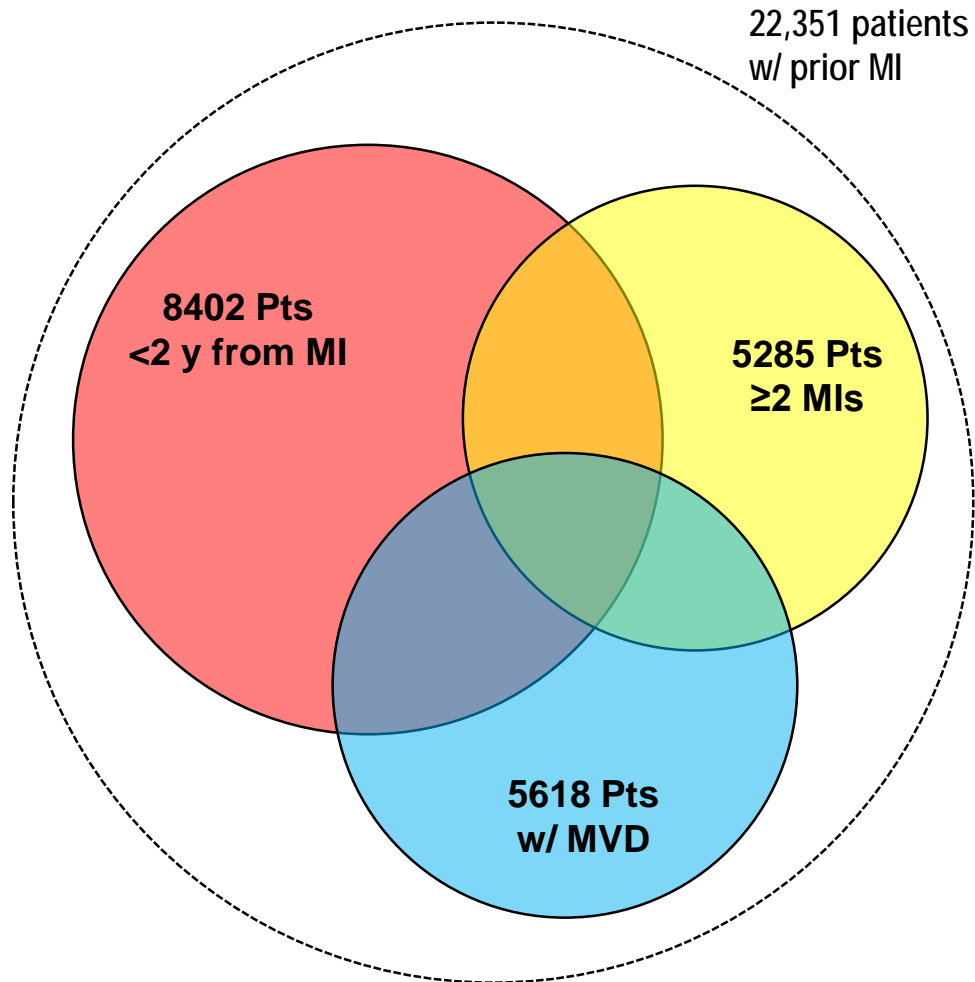


## No Multivessel Disease



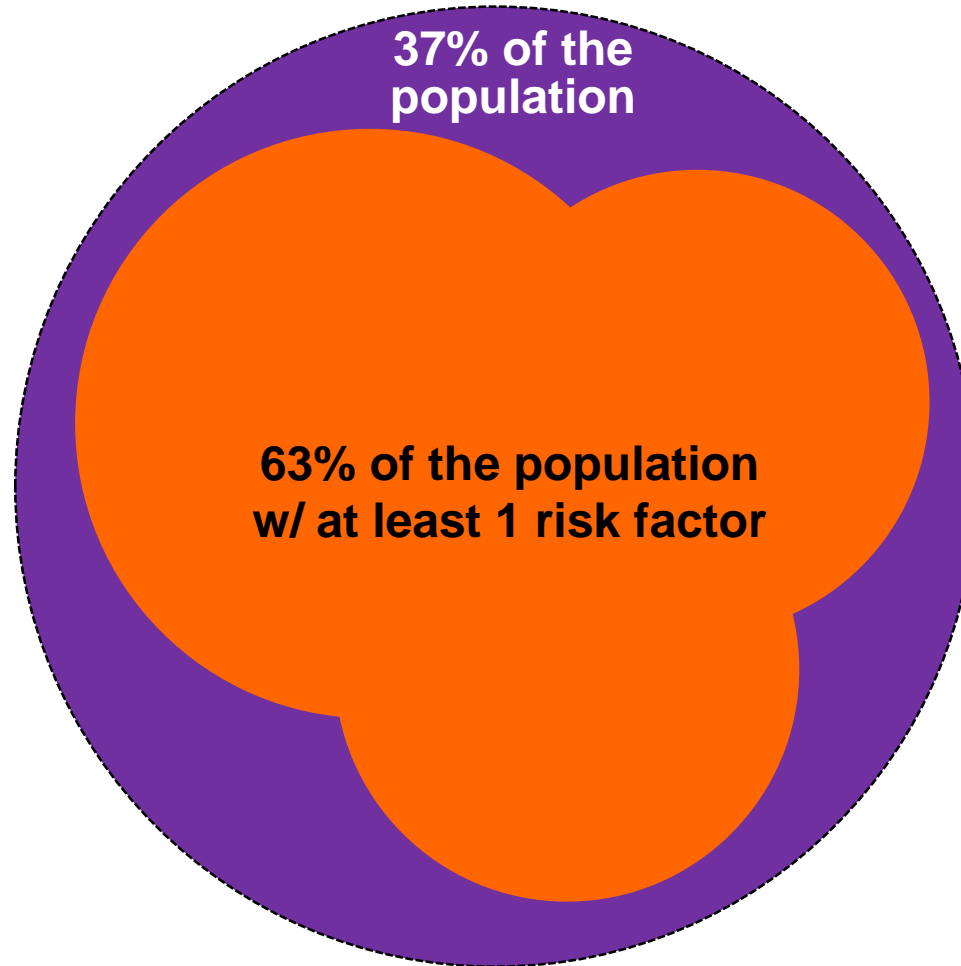


# Overlap Between Factors



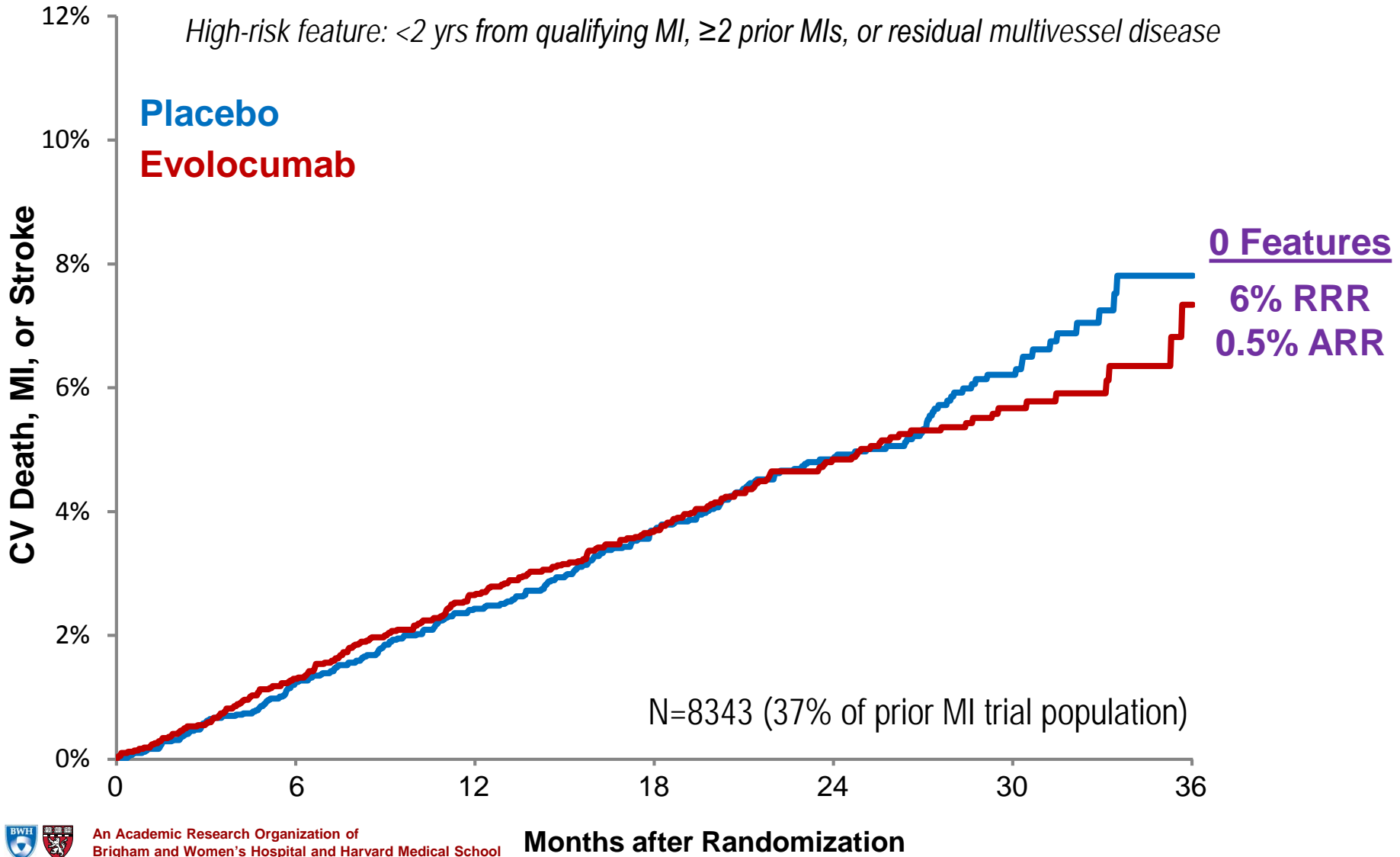


# Overlap Between Factors





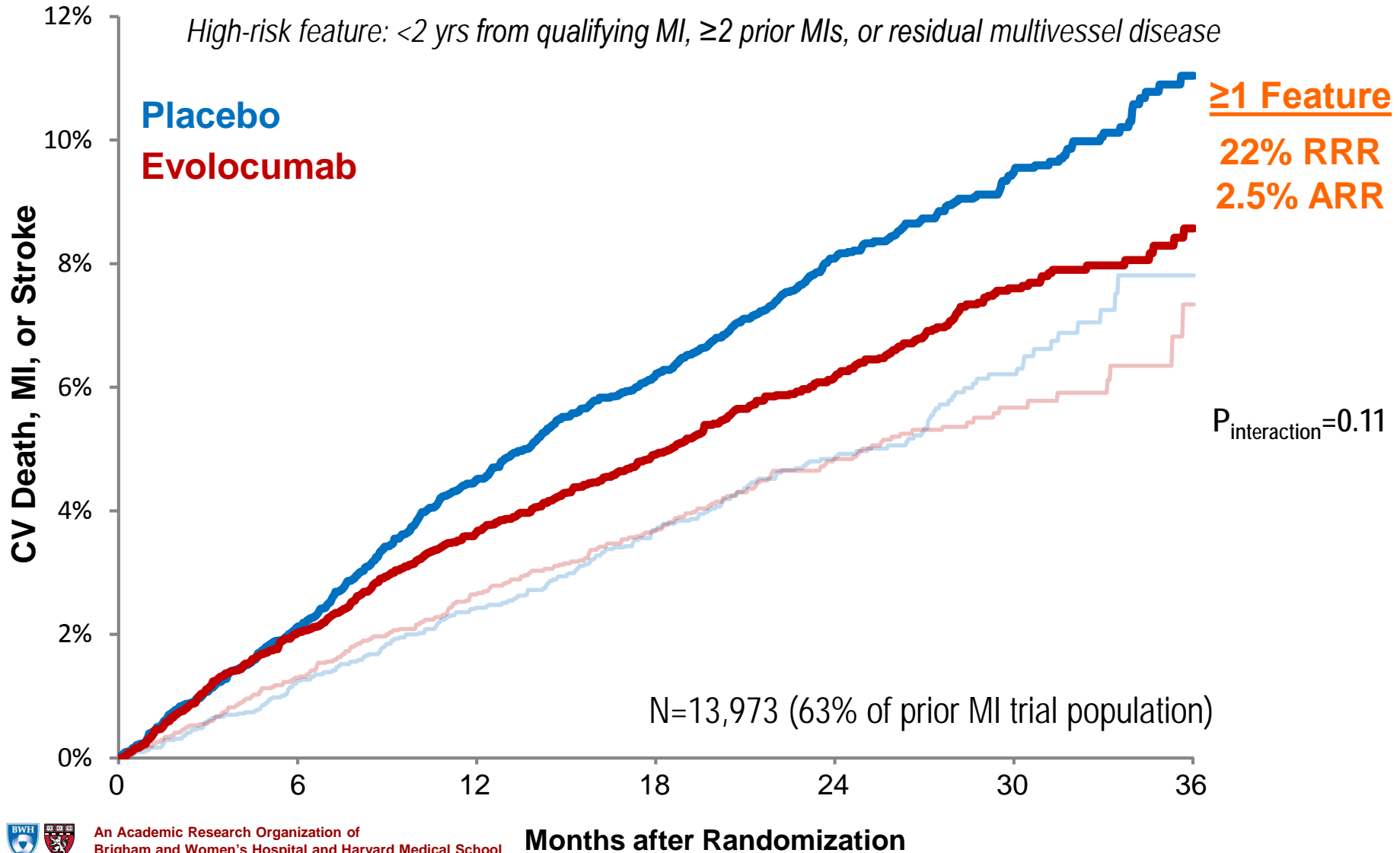
# Benefit of EvoMab Based on # of High-Risk MI Features





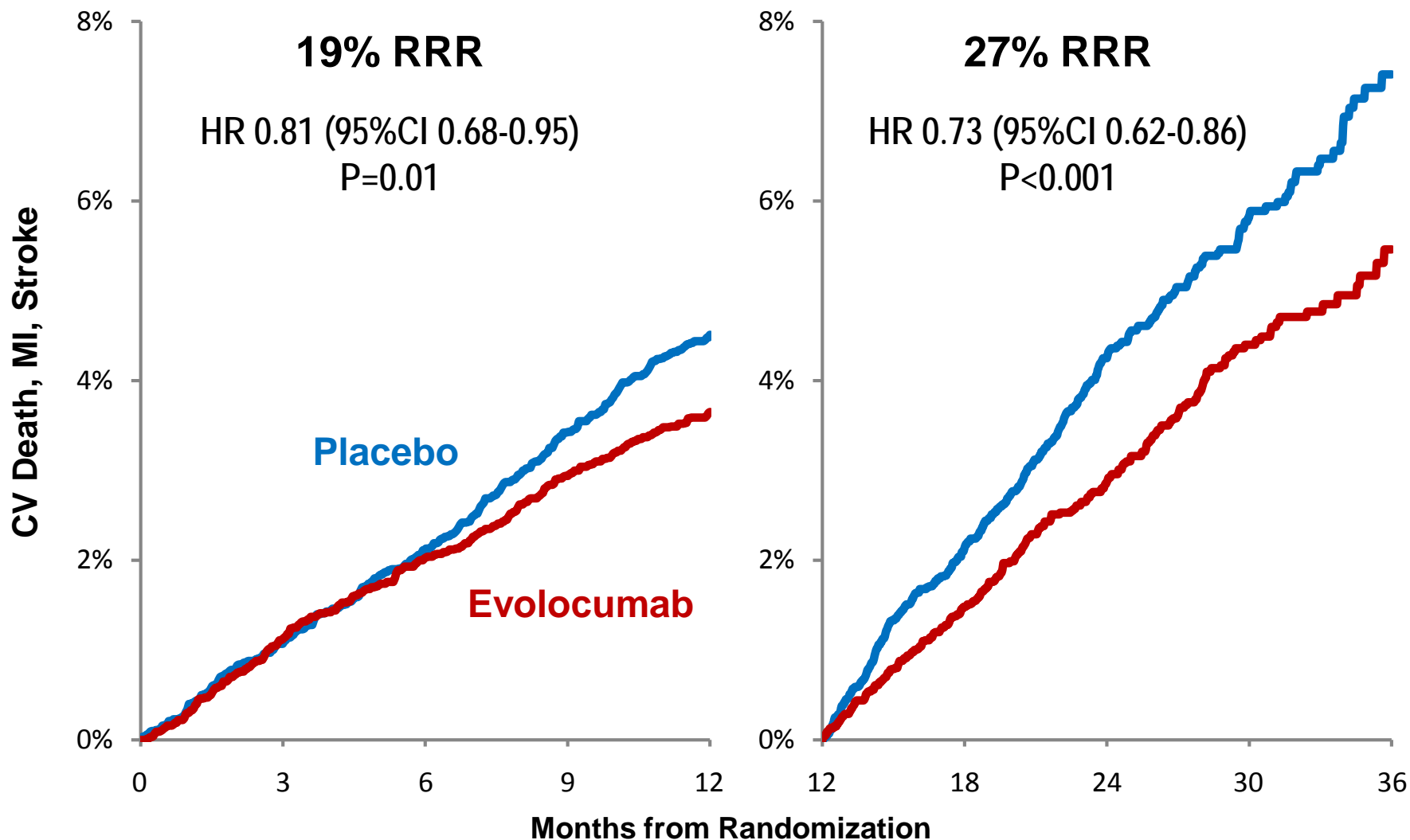


# Benefit of EvoMab Based on # of High-Risk MI Features



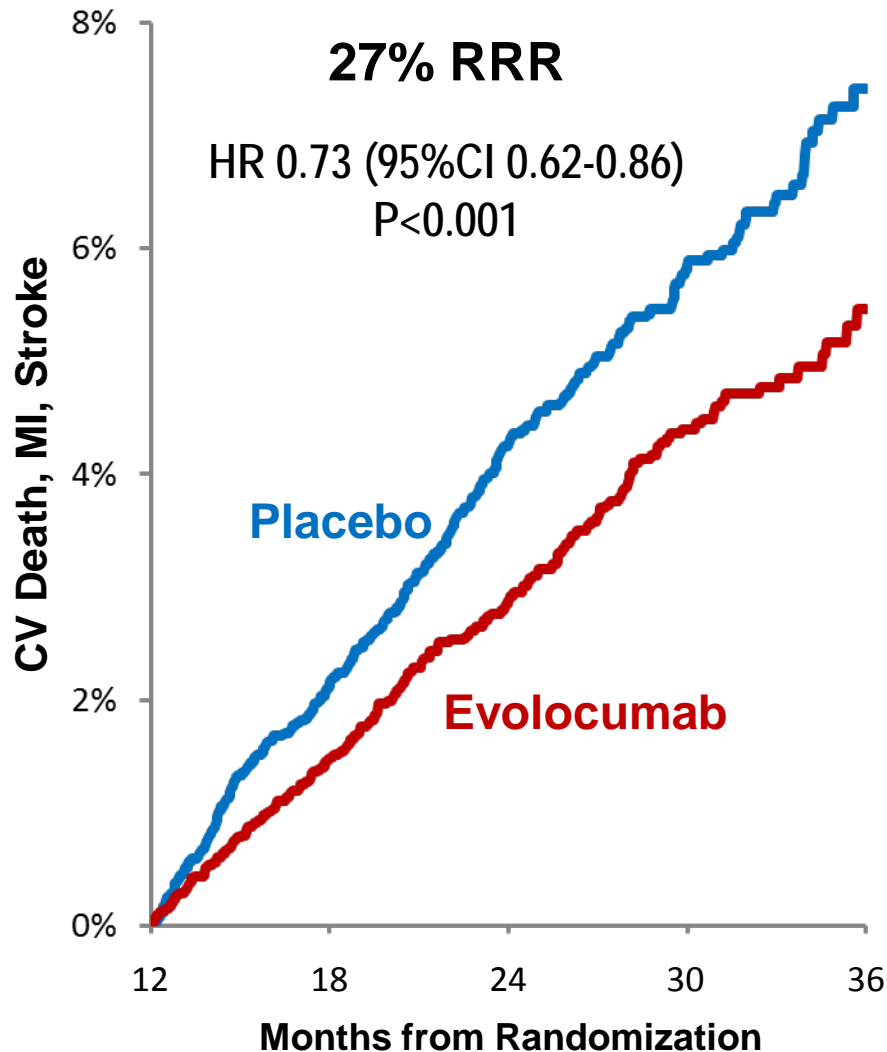


# Landmark Analyses in Pts w/ a High-Risk MI Feature





# Landmark Analyses in Pts w/ a High-Risk MI Feature



2% absolute risk reduction over 2 years

If same pattern continues, would extrapolate to 5% ARR over 5 years

NNT<sub>5y</sub> of ~20





# Summary



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- **Patients (1) closer to their most recent MI, (2) with multiple prior MIs, or (3) with multivessel disease are at 34-90% ↑ risk for major vascular events**
  - **These patients experience substantial:**
    - **relative risk reductions (21-30%) and**
    - **absolute risk reductions (2.6-3.4% over 3 yrs)****with intensive LDL-C lowering w/ the PCSK9i evolocumab**

***These readily ascertainable clinical features offer one approach to tailoring therapy***

